

Atty's Docket: 10,197.1  
N user et al.  
USSN 09/402,737

action analgesics are physically separated from each other. Accordingly, allowance of claim 9 is requested.

Further, in accordance with allowance of claim 9, new claims 16-20, and 23-27 are also distinct from Nelson and should be allowed for similar reasons.

Claims 21 and 22, are independent claims, each one reciting the Markush groups in allowed claim 10. Allowance of claims 21 and 22 is believed proper.

Claims 1-9, 12, 13 and 15 are held rejected in view of Examiner's belief that they are obvious in view of Nelson.

**NELSON'S TEACHING HAS BEEN SHOWN TO BE FALSE AND IS THEREFORE NOT  
ENTITLED TO THE PROBABLY WEIGHT AFFORDED BY EXAMINER**

In responding to the previous amendment, Examiner states that Nelson teaches that *it was once a longstanding belief that dextromethorphan had no significant analgesic activity, however, it has now been discovered...* See office action, section 4. Thus, Examiner apparently believes that the state of the art *prior* to Nelson, was that dextromethorphan had no analgesic properties, and that Nelson had disclosed that the state of the art had *subsequently* changed. This is not a correct interpretation of the chronology of the events.

The previously submitted excerpt from Basic and Clinical Pharmacology was published almost 10 years *after* Nelson filing date. Thus, Examiner's apparent belief that Nelson has modified the state of the art with respect to dextromethorphan's properties as an analgesic, is respectfully, not accurate.

Respectfully, we point out that Basic and Clinical Pharmacology was published in 1992, while Nelson was filed in 1982. If anything, this proves that the state of the art at the time of the filing date of the instant application was that dextromethorphan did not have analgesic properties.

Atty's Docket: 10,197.1  
Neuser et al.  
USSN 09/402,737

This state of the art is still the case as evidenced by the exhibit submitted herewith.

In the office action of 8/27/02, paper 24, Examiner maintained the rejection by arguing that terms such as "essentially free of analgesic properties" did not mean that there were zero analgesic properties. Thus, Examiner maintained the rejection although Nelson did not provide any support or evidence indicating that dextromethorphan has analgesic properties. Thus, his statement at col. 1, lines 60-65 and reproduced below, should not be accorded the weight provided by Examiner. Nelson writes:

Dextromethorphan (d-3-methoxy-N-methylmorphinan) is the d-isomer of the codeine analog of levorphanol; however, unlike the l-isomer, it has consistently been reported by the prior art as having no significant analgesic properties. (Emphasis added).

Examiner's attention is respectfully directed to the accompanying exhibit consisting of pages from the 10th edition of The Pharmacological Basis of Therapeutics, published and revised in 2001, and edited by Gilman, et al.

On the fourth page of the exhibit there is indicated near the bottom of column 2, a subheading **Dextromethorphan**. This section contains, *verbatim*, almost all of Nelson's statement. The only difference is that Nelson changed the conclusion's phrasing to make it sound less emphatic, and thus, give his application more credence. The sentence in the treatise is reproduced below and clearly states that, as of 2001 (Applicants' filing date), dextromethorphan had no analgesic properties.

Dextromethorphan (d-3-methoxy-N-methylmorphinan) is the d-isomer of the codeine analog of levorphanol; however, unlike the l-isomer, it has no analgesic or addictive properties and does not act through opioid receptors.

Examiner is respectfully reminded that the cited edition of Gilman et al., was published 19 years after Nelson's filing date. Therefore, even if Examiner accurately concludes from Nelson that in 1982 it was once a *longstanding belief that dextromethorphan had no significant analgesic activity, however, it has now been discovered...*, this was clearly not the state of the art at the time of filing the instant application.

Atty's Docket: 10,197.1  
Neuser et al.  
USSN 09/402,737

There are two possible conclusions gleaned from this comparison.

- ☒ Either Nelson "softened" Gilman's emphatic conclusion, and thus, misrepresented the state of the art to the PTO for his obvious reasons; or
- ☒ Nelson indeed, accurately copied Gilman's statement as it appeared. But that state of the art was subsequently altered with more recent evidence indicating that dextromethorphan has no analgesic properties.

Either possibility should cast significant doubt about the scientific veracity of Nelson's disclosure of dextromethorphan's properties.

In addition, the Applicants have provided excerpts from highly credible treatises indicating that dextromethorphan has no analgesic properties. These book chapters reviewed the literature from 1992 to 2001 – i.e., the contributions of the entire field.

Examiner must be asked to reconsider this evidence from the perspective of persons with ordinary skill in the art. Nelson's disclosure does not have [a] any data; [b] does not have any examples; and [c] does not even provide a single reference for his conclusions.

Is It Examiner's position that upon reviewing the evidence of record, that persons of ordinary skill would reasonably conclude that they could administer dextromethorphan and have a reasonable expectation of obtaining an analgesic effect?

The Applicants respectfully suggest that the answer must be in the negative, and that the rejection should be withdrawn.

Atty's Docket: 10,197.1  
Neuser et al.  
USSN 09/402,737

**NELSON DOES NOT PROVIDE AN ENABLING DISCLOSURE**

It is well established that a proper reference under 35 USC §§102 or 103 must be enabling in the sense of 35 USC §112, ¶1. It is suggested that Nelson is not enabling to that extent. Pertinent is the following quote from *In re Le Grice*, 133 USPQ 365, 374 (CCPA 1962):

"[T]he proper test of a description in a publication as a bar to a patent as the clause is used in section 102(b) requires a determination of whether one skilled in the art to which the invention pertains *could take the description of the invention in the printed publication and combine it with his own knowledge of the particular art and from this combination be put in possession of the invention* on which a patent is sought. [Emphasis added.]"

See also, *In re Hoeksema*, 158 USPQ 596, 601 (CCPA 1968), wherein the Court stated:

"While *In re Le Grice* was bottomed on an issue arising under 35 U.S.C. 102 where the reference was a 'printed publication,' that test, in our view, is also properly applicable to issues arising under 35 U.S.C. 103."

The rejection should be withdrawn because the foregoing remarks show that Nelson cannot reasonably be viewed as providing an enabling reference for making or practicing the instant claims.

A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). MPEP § 2121.01 Use of Prior Art in Rejections Where Operability Is In Question.

It is respectfully suggested that at the Applicants' filing date, person's with ordinary skill in the art could not have been in possession of Nelson's "invention" because the knowledge in the art was that dextr methorphan had no analgesic properties.

Atty's Docket: 10,197.1  
Neuser et al.  
USSN 09/402,737

Nelson even concedes that the mechanism of dextromethorphan's analgesic action is not fully understood. Col. 4, lines 18-24. Applicants suggest that this is because no such action existed.

In sum, persons of ordinary skill could not have used Nelson to describe the claimed subject matter. Put another way, in view of the foregoing remarks, it is not reasonable to maintain any rejection predicated on the belief that Nelson has placed the claimed subject matter in the public's possession.

In accordance with these remarks, withdrawal of the rejection is proper.

**NELSON DOES NOT TEACH EACH OF THE CLAIM LIMITATIONS**

The claims explicitly recite that the preparation must have one rapid onset of action, and one sustained action component.

Nowhere does Nelson describe dextromethorphan's alleged action to be either of a rapid onset type and locally acting, or a sustained acting type and systemic. Thus, it would not be clear from reading the text in col. 1, lines 48-56, which of these alleged analgesic combinations is actually rendering the instant claims obvious because they only require that dextromethorphan be present.

It is further noteworthy, that Nelson's claims encompass the use of dextromethorphan alone, by itself, for mouth pain. No examples were provided, and no descriptions were disclosed.

Further, the dextromethorphan composition is disclosed and claimed as being administered in a tablet form or an elixir. In the absence of evidence to the contrary, if the dextromethorphan is in a tablet, it must function systemically with sustained action. In addition, any other active agent in the tablet would also necessarily function systemically.

Atty's Docket: 10,197.1  
Neuser et al.  
USSN 09/402,737

If dextromethorphan is administered through an elixir, it would be rapidly absorbed by the rich supply of blood vessels in the oral cavity. This "buccal" mode of administration is quite common. Is the dextromethorphan provided by the elixir functioning systemically, or would dextromethorphan have local and rapid onset effects under these circumstances? One with skill in the art could not answer this question.

In maintaining the rejection, is Examiner suggesting that dextromethorphan corresponds to the instantly claimed element A or element B?

Is Nelson's combination of dextromethorphan and his group (1) conventional analgesics the equivalent of Applicants element A and element B, or is it simply a combination of 2 different sustained action, systemically acting compounds?

Or is Nelson's combination of dextromethorphan and his group (2) conventional anesthetics, the equivalent of Applicants element A and element B, or is it simply a combination of 2 different rapid onset, locally acting compounds?

It is respectfully suggested that if one in the art could not determine which of Nelson's proposed combinations are the equivalent of Applicants' combination of element A and element B, the rejection must be withdrawn. This is because without being able to answer the question, each limitation is not taught. At best, Nelson's disclosure would be obvious to try, even if dextromethorphan had analgesic properties.

It is submitted that without Nelson providing sufficient disclosure to answer these questions, Nelson cannot be viewed as reasonably describing each limitation in the claims. Nor does his specification provide guidance sufficient to be considered enabling as required.

Respectfully, the rejections over Nelson should be withdrawn.

Atty's Docket: 10,197.1  
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USSN 09/402,737

### CONCLUSIONS

Applicants appreciate the presumed validity of an issued patent. However, a patent's disclosure is merely a reflection of an applicant's view of the state of the art at the time the application is filed. A patent disclosure, like any technical document, must be considered in light of newly obtained and widely accepted evidence.

For example, Examiner's perspective would have substantially more force and reason if the Applicants' filing date were in the 1980's. At that time, Nelson's disclosure may have indeed, represented a new wave of knowledge just beginning to bear fruit. However, with the passage of almost 20 years since Nelson issued, and in the face of overwhelming evidence indicating Nelson's error, Examiner's acceptance of Nelson's disclosure would not be viewed as reasonable by others in the art.


Applicants have even indicated that it is likely that Nelson modified the force of Gilman's conclusion about dextromethorphan to advance his goals.

It has also been shown that even if dextromethorphan did have some analgesic properties (which we do not believe or concede at all) Nelson still could not render the instant claims obvious. This is because Nelson's omission of any disclosure as to how dextromethorphan actually would work means persons in the art cannot predict whether it is more like element A or more like element B of the instant claims. Thus, there is no suggestion of the claims. At best, there is an invitation to experiment – i.e., obvious to try.

Allowance of the claims is respectfully solicited.

Respectfully Submitted,

Norris, McLaughlin & Marcus  
220 East 42nd Street  
New York, NY 10017  
Telephone (212) 808-0700  
Facsimile (212) 808-0844

  
Theodore Gottlieb, PhD  
Reg. Nr. 42,597